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To: Bao-thuy Nguyen **Location:** REM-3C70 **Art Unit:** 1641 **Wednesday, February 25, 2004** **Case Serial Number:** 09/700643	**From:** Beverly Shears **Location:** Remsen Bldg. RM 1A54 **Phone:** 571-272-2528 beverly.shears@uspto.gov

3D51

Search Notes

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: _____ Serial Number: _____

Date: _____ Phone: _____ Art Unit: _____

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

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Date completed: 02-25-04
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CPU time: _____
Total time: 30
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_____ N.A. Sequence
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_____ Structure
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Vendors

_____ IG
✓ STN
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_____ Geninfo
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_____ DARC/Questel
✓ Other CGN

PTO-1590 (9-90)

Nguyen, B.
09/700643

FILE 'REGISTRY' ENTERED AT 08:55:29 ON 25 FEB 2004
L1 1 S CAWYASRGIRPVGR/SQSP

Seq.

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 251323-80-5 REGISTRY
CN L-Phenylalanine, L-cysteinyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6: PN: WO9960112 SEQID: 7 claimed sequence
SQL 15

SEQ 1 CAWYASRGIR PVGRF
========== ====
HITS AT: 1-14

REFERENCE 1: 132:11632

FILE 'HCAPLUS' ENTERED AT 08:56:10 ON 25 FEB 2004
L2 1 S L1

L2 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 Nov 1999
ACCESSION NUMBER: 1999:753334 HCAPLUS
DOCUMENT NUMBER: 132:11632
TITLE: Monoclonal antibody to ligand 19P2 and its therapeutical use
INVENTOR(S): Matsumoto, Hirokazu; Kitada, Chieko; Hinuma, Shuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9960112	A1	19991125	WO 1999-JP2650	19990520
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2328416	AA	19991125	CA 1999-2328416	19990520
AU 9937331	A1	19991206	AU 1999-37331	19990520
JP 2000037187	A2	20000208	JP 1999-140305	19990520
EP 1081222	A1	20010307	EP 1999-919662	19990520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1998-140293 A 19980521
WO 1999-JP2650 W 19990520

Searcher : Shears 571-272-2528

AB Provided is a mouse IgG-type monoclonal antibody (in particular, P2L-1Ca) highly reactive to ligand 19P2 and being capable of neutralizing the arachidonic acid metabolite-releasing activity of ligand 19P2. Thus, the antibody can be used as a diagnostic, prophylactic, or therapeutic agent for various diseases associated with the ligand 19P2-associated pituitary function regulatory mechanism (e.g., promotion of the prolactin secretion), the central nerve regulatory mechanism, the pancreatic function regulatory mechanism, etc. Furthermore, the monoclonal antibody can be used for the determination of ligand 19P2 or its derivs. by the sandwich immunoassay, especially by using the antibody recognizes the middle portion of the ligand. This assay method is useful for the study of the physiol. functions of ligand 19P2 and its derivative Preparation of antigenic fragments of human, rat, and bovine ligand 19P2; preparation of IgG-type mouse monoclonal antibodies P2L-1Ca and P2L-2Ca to ligand 19P2; and use of the monoclonal antibodies for the determination of ligand 19P2 by sandwich-EIA were demonstrated.

IT **251323-80-5P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human ligand 19P2 fragment (residues 17-31) as antigen; monoclonal antibody to ligand 19P2 and therapeutical use)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'HCAPLUS' ENTERED AT 08:56:10 ON 25 FEB 2004)

```
L3          6 S 19P2
L4          0 S ORPHAN G(S)CONJUGAT? RECEPTOR
L5        242 S ORPHAN G
L6        241 S L5(S)PROTEIN
L7        241 S L6(S)RECEPTOR
L8          0 S L7(S)CONJUGAT?
L9          5 S L3 NOT L2
```

- key terms

L9 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 18 Jan 1999
ACCESSION NUMBER: 1999:32028 HCAPLUS
DOCUMENT NUMBER: 130:94530
TITLE: Method of producing a 19p2 ligand/prolactin-releasing peptide by cleavage of a recombinant fusion protein
INVENTOR(S): Suenaga, Masato; Moriya, Takeo; Tanaka, Yoko; Nishimura, Osamu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 887417	A2	19981230	EP 1998-111725	19980625
EP 887417	A3	19990113		

Searcher : Shears 571-272-2528

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

CA 2242086	AA	19981227	CA 1998-2242086	19980626
JP 11071396	A2	19990316	JP 1998-180555	19980626
US 6103882	A	20000815	US 1998-105678	19980626
US 6258561	B1	20010710	US 1999-421208	19991020

PRIORITY APPLN. INFO.: JP 1997-172118 A 19970627
JP 1997-17218 A 19970627
US 1998-105678 A3 19980626

AB The method of the present invention is suitable for the com. high-level production of a protein or peptide which can be used as a prophylactic and therapeutic drug. Thus, plasmid pTB960-10, containing a chimeric gene encoding prolactin-releasing peptide fused to the N-terminus of cysteinyl-basic fibroblast growth factor, was prepared Escherichia coli transformed with this plasmid was used to prepare the peptide. The peptide was released from the fusion protein by a process comprising cyanylation followed by hydrolysis or ammonolysis.

L9 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 17 Nov 1998
ACCESSION NUMBER: 1998:728552 HCAPLUS
DOCUMENT NUMBER: 130:836
TITLE: An endogenous pituitary-derived protein ligand for a G protein-coupled receptor, a cDNA encoding it, and their therapeutic uses
INVENTOR(S): Hinuma, Shuji; Fukusumi, Shoji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849295	A1	19981105	WO 1998-JP1923	19980427
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9870817	A1	19981124	AU 1998-70817	19980427
JP 11009286	A2	19990119	JP 1998-117189	19980427
EP 981616	A1	20000301	EP 1998-917693	19980427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002143152	A1	20021003	US 2002-44592	20020110

PRIORITY APPLN. INFO.: JP 1997-109974 A 19970428
WO 1998-JP1923 W 19980427
US 1999-403639 A2 19991025

AB A ligand for an orphan G protein-coupled receptor of the mouse pituitary gland is identified and a cDNA encoding it is cloned. The

receptor and its ligand may be targets for the development of therapeutic agents for a number of mental disorders and diseases of the pancreas. The receptor cDNA was cloned by PCR using primers derived from conserved sequences of G protein-coupled receptors. Individual PCR products were cloned and sequenced and the sequences screened for extended homol. to other G protein-coupled receptors. The cDNA was expressed in CHO cells using the pAKKO-111H vector system. Cells expressing the receptor gene were then used to assay for factors stimulating arachidonic acid metabolite release in rat brain exts. An activity was detected after fractionation and an activity showing the same properties was found in cattle brain exts. and purified to homogeneity. Three peaks of activity were found and characterized. CDNAs were cloned by RT-PCR. Biol. activity of the peptides was confirmed using chemical synthesized peptides.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1973:426322 HCAPLUS
DOCUMENT NUMBER: 79:26322
TITLE: Application of delayed neutron spectrometry to nuclear materials assay
AUTHOR(S): Shaley, S.
CORPORATE SOURCE: Dep. Nucl. Sci., Tech. Israel Inst. Technol., Haifa, Israel
SOURCE: Nuclear Materials Management (1972), 1(3), 291-8
CODEN: NUMMB8; ISSN: 0362-0034
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The energy distribution of delayed n is used in a nondestructive anal. technique to identify nuclear materials. By employing active interrogation, fissile materials can be identified with a high degree of precision and in an unambiguous fashion. This assay technique is based on the recent measurement of delayed n energy spectra from fissile materials by S. (19pj) and S. and G. Rudstam (**19p2**).

L9 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1973:424761 HCAPLUS
DOCUMENT NUMBER: 79:24761
TITLE: S-type current-voltage characteristic in Gunn diodes
AUTHOR(S): Gel'mont, B. L.; Shur, M. S.
CORPORATE SOURCE: A. F. Ioffe Phys. Tech. Inst., Leningrad, USSR
SOURCE: Journal of Physics D: Applied Physics (1973), 6(7), 842-50
CODEN: JPAPBE; ISSN: 0022-3727
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rate of impact ionization in the high-field Gunn domain is derived. The threshold voltage of the neg.-slope region of the S-type current-voltage characteristic is determined The limitations of the Gunn diode parameters by impact ionization are discussed. The

process of the violation of the Gunn current waveform coherence under impact-ionization conditions is calculated The theory agrees well with the exptl. data; the criterion of the validity of the theory was not taken into account in the paper of Southgate (**19p2**), which was devoted to the comparison of the simplified version of the theory with the experiment

L9 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1973:424109 HCAPLUS
DOCUMENT NUMBER: 79:24109
TITLE: Heats of solution of gaseous anilinium and pyridinium ions in water and intrinsic basicities in aqueous solution
AUTHOR(S): Taft, R. W.; Taagepera, M.; Summerhays, K. D.; Mitsky, J.
CORPORATE SOURCE: Dep. Chem., Univ. California, Irvine, CA, USA
SOURCE: Journal of the American Chemical Society (1973), 95(11), 3811-12
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With NH3 as the reference base, the relative standard heats of solution in water, measured and defined as previously described (E. M. Arnett, et al., 1972), were $-\Delta Hs^{\circ}$ = 76.0, 64.0, and 62.0 kcal/mole for PhNH3+(g), gaseous pyridinium cation, and gaseous 4-methylpyridium cation, resp. Comparison of the aromatic N conjugate acids with their corresponding saturated members showed that the standard Gibbs free energy change (ΔGi°) for ionization either in aqueous solution or in the gas phase (M. T., et al., **19p2**) was 7-10 kcal/mole more neg. for the aromatic member than for the saturated member of the pair. The ΔGi° values for the aromatic members were 10-20% less neg. in water than in the gas phase.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 08:58:51 ON 25 FEB 2004)
L10 6 S L3
L11 3 S L8

L14 2 S L11 AND LIGAND
L15 8 S L10 OR L14
L16 8 DUP REM L15 (0 DUPLICATES REMOVED)

L16 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:380731 BIOSIS
DOCUMENT NUMBER: PREV200100380731
TITLE: Method of producing a **19P2** ligand.
AUTHOR(S): Masato, Suenaga [Inventor, Reprint author]; Takeo, Moriya [Inventor]; Yoko, Tanaka [Inventor]; Osamu, Nishimura [Inventor]
CORPORATE SOURCE: Hyogo, Japan
ASSIGNEE: Takeda Chemical Industries, Ltd., Osaka, Japan
PATENT INFORMATION: US 6258561 July 10, 2001
SOURCE: Official Gazette of the United States Patent and

Searcher : Shears 571-272-2528

Trademark Office Patents, (July 10, 2001) Vol. 1248, No. 2. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Aug 2001
Last Updated on STN: 19 Feb 2002

AB The method of the present invention is suitable for the commercial high-level production of a protein or peptide which can be used as a prophylactic and therapeutic drug for various diseases such as senile dementia, cerebrovascular dementia (dementia arising from cerebrovascular disorders), dementia associated with genealogical retroplastic diseases (e.g. Alzheimer's disease, Parkinson's disease, Pick's disease, Huntington's disease, etc.), dementia associated with infectious diseases (e.g. Creutzfeldt-Jakob's and other virus diseases), dementia associated with endocrine or metabolic disease or toxicosis (e.g. hypothyroidism, vitamin B12 deficiency, alcoholism, intoxication by drugs, metals, and organic compounds), dementia associated with tumorigenic diseases (e.g. brain tumor), dementia associated with traumatic diseases (e.g. chronic subarachnoidal hemorrhage), and other types of dementia, depression, hyperactive child syndrome (microencephalopathy), and disturbance of consciousness. Additionally, the ligand polypeptide of the present invention has prolactin secretion-stimulating and -inhibiting activities.

L16 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:191023 BIOSIS
DOCUMENT NUMBER: PREV200100191023
TITLE: Method of producing a **19P2** ligand.
AUTHOR(S): Masato, Suenag [Inventor, Reprint author]; Takeo, Moriya [Inventor]; Yoko, Tanaka [Inventor]; Osamu, Nishimura [Inventor]
CORPORATE SOURCE: Hyogo, Japan
ASSIGNEE: Takeda Chemical Industries, Ltd., Osaka, Japan
PATENT INFORMATION: US 6103882 August 15, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 15, 2000) Vol. 1237, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 2001
Last Updated on STN: 18 Feb 2002

AB The method of the present invention is suitable for the commercial high-level production of a protein or peptide which can be used as a prophylactic and therapeutic drug for various diseases such as senile dementia, cerebrovascular dementia (dementia arising from cerebrovascular disorders), dementia associated with genealogical retroplastic diseases (e.g. Alzheimer's disease, Parkinson's disease, Pick's disease, Huntington's disease, etc.), dementia associated with infectious diseases (e.g. Creutzfeldt-Jakob's and other virus diseases), dementia associated with endocrine or metabolic disease or toxicosis (e.g. hypothyroidism, vitamin B12

deficiency, alcoholism, intoxication by drugs, metals, and organic compounds), dementia associated with tumorigenic diseases (e.g. brain tumor), dementia associated with traumatic diseases (e.g. chronic subarachnoidal hemorrhage), and other types of dementia, depression, hyperactive child syndrome (microencephalopathy), and disturbance of consciousness. Additionally, the ligand polypeptide of the present invention has prolactin secretion-stimulating and inhibiting activities.

L16 ANSWER 3 OF 8 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-039381 [03] WPIDS
DOC. NO. NON-CPI: N2000-029673
DOC. NO. CPI: C2000-010308
TITLE: New monoclonal antibodies, useful in diagnosis, as drugs and in studying diseases related to ligand abnormality.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HINUMA, S; KITADA, C; MATSUMOTO, H
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9960112	A1	19991125	(200003)*	JA	73
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU ZA					
JP 2000037187	A	20000208	(200018)		30
AU 9937331	A	19991206	(200019)		
EP 1081222	A1	20010307	(200114)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2000549720	X	20021112	(200275)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9960112	A1	WO 1999-JP2650	19990520
JP 2000037187	A	JP 1999-140305	19990520
AU 9937331	A	AU 1999-37331	19990520
EP 1081222	A1	EP 1999-919662	19990520
		WO 1999-JP2650	19990520
JP 2000549720	X	WO 1999-JP2650	19990520
		JP 2000-549720	19990520

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9937331	A	Based on	WO 9960112
EP 1081222	A1	Based on	WO 9960112
JP 2000549720	X	Based on	WO 9960112

PRIORITY APPLN. INFO: JP 1998-140293 19980521
AN 2000-039381 [03] WPIDS
AB WO 9960112 A UPAB: 20000118
NOVELTY - A monoclonal antibody which has a specific reaction with the part peptide of the C-terminal of **19P2** ligand or its derivative is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for (1) another monoclonal antibody that has specific reaction with the middle peptide of **19P2** ligand or its derivative;
(2) a quantitation method for **19P2** or its derivative in a specimen solution by using either or both of the monoclonal antibodies;
(3) a hybridoma cell can produce the monoclonal antibody.
ACTIVITY - Neutralizing arachidonic acid metabolite-releasing activity of **19P2** ligand; diagnosis and treating **19P2** related diseases; clarifying physiological functions of **19P2** ligand and its derivative.
MECHANISM OF ACTION - Antibody.
USE - The antibodies can be used in diagnosis or to treat or prevent diseases associated with abnormality in the pituitary function regulatory mechanism (e.g. promotion of prolactin secretion), central nervous regulatory mechanism, and pancreatic function regulatory mechanism. The antibody-based immunoassay can also be applied in clarifying the physiological functions of the ligand and its derivative.
DESCRIPTION OF DRAWING(S) - Increase of antibody potency in all 8 immunized mice shown against **19P2** ligand.
Antiserum dilution (1/1000) a
Dwg.1/14

L16 ANSWER 4 OF 8 JAPIO (C) 2004 JPO on STN
ACCESSION NUMBER: 1999-071396 JAPIO
TITLE: PRODUCTION OF **19P2** LIGAND
INVENTOR: SUENAGA MASATO; MORIYA TAKERO; TANAKA YOKO; NISHIMURA TADASHI
PATENT ASSIGNEE(S): TAKEDA CHEM IND LTD
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 11071396	A	19990316	Heisei	C07K014-47

APPLICATION INFORMATION
STN FORMAT: JP 1998-180555 19980626
ORIGINAL: JP10180555 Heisei
PRIORITY APPLN. INFO.: JP 1997-172118 19970627
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 1999
AN 1999-071396 JAPIO
AB PROBLEM TO BE SOLVED: To industrially and advantageously produce the subject compound useful for the treatment or the like of senile dementia or the like by subjecting a fusion protein or the like prepared by connecting a protein or the like having cysteine at the N-terminal to a **19P2** ligand to a cleavage reaction on the N side of the cysteine residue.
SOLUTION: A transformant holding a vector having a gene capable of

coding a fusion protein or peptide prepared by connecting **19P2** ligand to the N-terminal of a protein or a peptide having cysteine at the N-terminal to a **19P2** ligand is cultured to express the fusion protein or peptide and the expressed fusion protein or peptide is subjected to a cleavage reaction of the peptide bond on the amino group side of the cysteine residue by cyanation reaction and then an ammonolysis or a hydrolytic reaction. Thereby, the objective **19P2** ligand useful for prevention, treatment or the like of senile dementia, cerebrovascular dementia, dementia caused by systemic degenerative type retrograde disease and infectious disease, dysboulia, schizophrenia, hypercholeterolemia, acute cardiac infarction, atopic dermatitis or the like is industrially and advantageouly produced.

L16 ANSWER 5 OF 8 WPIDS
ACCESSION NUMBER: 1999-047884 [05] WPIDS
DOC. NO. CPI: C1999-015234
TITLE: Producing a **19P2** pituitary G protein receptor ligand - by cleavage of a fusion protein, useful for preventing and treating dementia, breast cancer, renal failure and autoimmune disease.
DERWENT CLASS: B04 D16
INVENTOR(S): MORIYA, T; NISHIMURA, O; SUENAGA, M; TANAKA, Y; MASATO, S; OSAMU, N; TAKEO, M; YOKO, T
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 887417	A2	19981230	(199905)*	EN	56
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 11071396	A	19990316	(199921)		37
CA 2242086	A	19981227	(199924)		
US 6103882	A	20000815	(200041)		
US 6258561	B1	20010710	(200141)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 887417	A2	EP 1998-111725	19980625
JP 11071396	A	JP 1998-180555	19980626
CA 2242086	A	CA 1998-2242086	19980626
US 6103882	A	US 1998-105678	19980626
US 6258561	B1 Div ex	US 1998-105678	19980626
		US 1999-421208	19991020

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6258561	B1 Div ex	US 6103882

PRIORITY APPLN. INFO: JP 1997-172118 19970627
AN 1999-047884 [05] WPIDS
AB EP 887417 A UPAB: 19990203
Producing a **19P2** (pituitary G protein-coupled receptor) ligand or amide or salt comprising subjecting a fusion protein or peptide comprising the **19P2** ligand fused to a protein or peptide having a cysteine residue at the N-terminus to a reaction for cleavage of the peptide bond on the amino terminal side of the cysteine residue (method I) is new. Also claimed are (1): a fusion protein or peptide comprising a **19P2** ligand fused to a protein or a peptide having a cysteine residue at its N-terminus; (2) a vector containing a gene coding for the fusion protein or peptide of (1); (3) a transformant habouring the vector of (2); and (4) a method as (I), additionally comprising culturing the transformant and cleaving the expressed fusion protein.

USE - The new method is useful for the commercial high level production of a protein or peptide which can be used as a prophylactic and therapeutic drug for various diseases including: senile dementia, cerebrovascular dementia, and dementia associated with: genealogical disorders (e.g. Alzheimer's disease, Parkinson's disease, Pick's disease, Huntington's disease), infectious diseases (e.g. Creutzfeldt-Jakob's), endocrine or metabolic disease or toxicosis (e.g. hypothyroidism, vitamin B12 deficiency, alcoholism, intoxication by drugs, metal and organic compounds), tumourigenic diseases (e.g. brain tumour), traumatic diseases (e.g. chronic subarachnoidal heamorrhage, and other types of dementia, depression, hyperactive child syndrome (microencephalopathy) and disturbance of consciousness. The **19P2** ligand polypeptide also has prolactin secretin-stimulating and -inhibiting activities, and so is useful for prevention and treatment of diseases associated with prolactin hypo and hypersecretion respectively, including: hyperprolactinaemia, pituitary adenoma, breast cancer, infertility, impotence and autoimmune disease (hypersecretion disorders), and seminal vesicle hypoplasia, osteoporosis, menopausal syndrome and renal failure (hyposecretion disorders). The **19P2** polypeptide/amide is also useful as a test reagent for study of the prolactin secretory function or a veterinary drug for use as a lactogogue in mammalian farm animals and harvesting of the substances secreted into their milk.

ADVANTAGE - The new method is highly efficient at producing **19P2** from a fusion protein, as the prior art cleavage methods were either incompatible with methionine-containing peptides (using cyanogen bromide), or low excision yield (using factor Xa).

L16 ANSWER 6 OF 8 JAPIO (C) 2004 JPO on STN
ACCESSION NUMBER: 2000-159798 JAPIO
TITLE: NEW PHYSIOLOGICALLY ACTIVE SUBSTANCE, THEIR MANUFACTURE AND USE
INVENTOR: HINUMA KUNIJI; TATSUMOTO KAZUHIKO; HOSOYA MASAKI; HABATAKE YUUGO; FUJII AKIRA; KITADA CHIEKO
PATENT ASSIGNEE(S): TAKEDA CHEM IND LTD
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC

JP 2000159798 A 20000613 Heisei C07K014-705

APPLICATION INFORMATION
STN FORMAT: JP 1998-364656 19981222
ORIGINAL: JP10364656 Heisei
PRIORITY APPLN. INFO.: JP 1997-353955 19971224
PRIORITY APPLN. INFO.: JP 1998-32577 19980216
PRIORITY APPLN. INFO.: JP 1998-220853 19980804
PRIORITY APPLN. INFO.: JP 1998-271645 19980925
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2000

AN 2000-159798 JAPIO
AB PROBLEM TO BE SOLVED: To obtain a new physiologically active substance which is a **ligand** to an **orphan G protein conjugate** type **receptor** APJ expressing in a central nervous system, circulatory system, immune system or the like useful for the central nervous system function modifier, circulatory function modifier, immunological function modifier or the like.
SOLUTION: This substance is a polypeptide having binding capacity to a receptor protein including same or practically same amino acid sequence to the amino acid sequence of the formula, it's precursor, their ester or salt. The subject polypeptide is, for example, is obtained in the processes, for example, purifying polypeptide from human tissue or cells, synthesizing the polypeptide in a known method, or culturing a transformant including a DNA coding for the polypeptide. The polypeptide is usable for quantitative analysis of APJ that is a G protein conjugating type receptor, development of receptor bonding assey system using recombination type receptor protein expressing system and screening of medicinae candidate compounds or the like.
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L16 ANSWER 7 OF 8 JAPIO (C) 2004 JPO on STN
ACCESSION NUMBER: 2000-159795 JAPIO
TITLE: PEPTIDE DERIVATIVE
INVENTOR: KITADA CHIEKO; HINUMA KUNIJI
PATENT ASSIGNEE(S): TAKEDA CHEM IND LTD
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 2000159795	A	20000613	Heisei	C07K014-00

APPLICATION INFORMATION
STN FORMAT: JP 1999-270419 19990924
ORIGINAL: JP11270419 Heisei
PRIORITY APPLN. INFO.: JP 1998-271626 19980925
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2000

AN 2000-159795 JAPIO
AB PROBLEM TO BE SOLVED: To obtain a new substance being a modified substance of natural type **ligand** against APJ being an **orphan G protein conjugated receptor** expressed in the central nervous system, circulatory system, immune system, etc., useful as a central nerve

function regulator, a circulatory function regulator, an immune function regulator, etc.
SOLUTION: This compound is shown by formula I (X1 is H, an amino acid or a peptide comprising 1-25 amino acids; X2 is a neutral amino acid; X3 is a neutral amino acid, an aromatic amino acid or the like; X4 is a direct bond, a neutral amino acid or the like; X5 is an amino acid derivative containing a C end reduced to formyl, a hydroxyl group or the like; with the proviso that cases in which X2 is Leu, X3 is Lys, X4 is Met, X5 is Pro or Pro-Phenol and each amino acid residue of -Arg-Pro-Arg-, -Ser-His- and -Glycol-pro- is nonsubstituted are omitted) such as a compound of formula II. The compound is obtained, for example, by obtaining a natural type **ligand** by a method for purifying a peptide from human or warm-blooded animal tissue or cell and modifying the **ligand**
.

L16 ANSWER 8 OF 8 JAPIO (C) 2004 JPO on STN
ACCESSION NUMBER: 2000-037187 JAPIO
TITLE: ANTIBODY AND ITS USE
INVENTOR: MATSUMOTO HIROKAZU; KITADA CHIEKO; HINUMA KUNITJI
PATENT ASSIGNEE(S): TAKEDA CHEM IND LTD
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 2000037187	A	20000208	Heisei	C12N015-02

APPLICATION INFORMATION
STN FORMAT: JP 1999-140305 19990520
ORIGINAL: JP11140305 Heisei
PRIORITY APPLN. INFO.: JP 1998-140293 19980521
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2000

AN 2000-037187 JAPIO
AB PROBLEM TO BE SOLVED: To obtain a new antibody which consists of a monoclonal antibody specifically reacting with a C-terminal partial peptide of **19P2** ligand (or its derivative), and can be used, for example, for determining **19P2** ligand, and diagnosing and treating diseases caused, for example, by abnormal regulation of pituitary.
SOLUTION: This is a new monoclonal antibody specifically reacting with a C-terminal partial peptide of **19P2** ligand or its derivative, and can be used, for example, for determining **19P2** ligand, and diagnosing and treating various diseases caused, for example, by troubles, for example, in 'pituitary function'- regulating action (e.g. 'prolactin secretion'-promoting action) which is considered to be possessed by **19P2** ligand, 'central nerve function'-regulating action, and 'pancreas function'-regulating action. This monoclonal antibody is obtained by administering **19P2** ligand prepared from a tissue or cell of a mammalian animal (e.g. human, monkey, or rat) by the conventional method to a warm- blooded animal (e.g. mouse) with an adjuvant for immunization, collecting an antibody-producing cell after the final immunization to fuse with a myeloma cell, culturing the fused cell in HAT medium to give a hybridoma, cloning the

obtained hybridoma, followed by culturing the obtained hybridoma.

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